PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Atrial Fibrillation in Indigenous and Non-Indigenous Australians: A Cross-Sectional Study
AUTHORS	Wong, Christopher; Brook, Anthony; Cheng, Yi Han; Lau, Dennis; Rangnekar, Geetanjali; Roberts-Thomson, Kurt; Kalman, Jonathan; Brown, Alex; Sanders, Prashanthan

VERSION 1 - REVIEW

REVIEWER	Hui-Nam Pak Yonsei University Health System, Seoul, Republic of Korea
REVIEW RETURNED	17-Aug-2014

GENERAL COMMENTS	Wong et al. conducted a retrospective cross sectional study which shows that Indigenous Australians with AF were younger, and had low left ventricular systolic function and greater rates of cardiovascular comorbidities than non-Indigenous Australians with AF. They concluded that the risk factor modification may mitigate the excess burden of morbidity and mortality due to AF in younger Indigenous Australians. This is a large population study included over 200,000 patients during over 10 years in spite of some limitations. Major comment 1. As the authors described, this study has limitations regarding to a selection bias, a discrepancies of number and characteristics of each group, diagnostic methods for AF and other structural heart disease, or omitting multiple strong comorbid factors associated with AF. Therefore, the authors need to mention that the results of this study could not be generalized. 2. This is the cross sectional observation study, and there is no data explaining the relationship between AF prevalence and morbidity/ mortality. Also, the terminology of “Predictor” in multivariable analysis should be changed to the “association”. The need for better primary prevention strategies is also speculative. The authors should tone down the conclusion based on the data. Minor Comments 1. Although the authors described the difference between Indigenous Australians and non-Indigenous Australians regarding to the medical aspects, the readers may have curiosity whether it is related to genetic factor or their life-style. I recommend discuss more about the characteristics for Indigenous Australians. 2. The logic of the authors seems to be Indigenous Australians are different to non-Indigenous Australians genetically, so that the prevalence of structural heart disease or remodeling are different,

	resulting in high prevalence of young age AF. Therefore, early intervention for primary prevention in this group will reduce the risk of AF and other cardiovascular conditions. However, there are too many steps of speculation to support this complicated logics. Propensity score matching of control group to Indigenous Australians may be helpful to support the authors' explanation with this precious large population data. 3. Did structural changes of hear induce AF, or AF induced structural remodeling of heart? Although it is not possible to document the causal-result relationship, please discuss about that.

REVIEWER	MANSOURATI, Jacques Département de Cardiologie Hôpital de la Cavale Blanche
REVIEW RETURNED	26-Sep-2014

GENERAL COMMENTS	This is a retrospective study with its limitations some additional clinical data may have been interesting. This paper brings interesting and original epidemiological results on AF in 2 australian populations. It may have preventive impact on Indigenious population according to the results. The study is however retrospective and has to be analyzed carefully It would have been interesting to have more clinical data on the studied populations as body mass index and alcohol consumption. Would that be still possible? These parameters may bring a possible explanation for the results

VERSION 1 – AUTHOR RESPONSE

Reviewer Name Hui-Nam Pak
Institution and Country Yonsei University Health System, Seoul, Republic of Korea
Please state any competing interests or state 'None declared': None declared

Wong et al. conducted a retrospective cross sectional study which shows that Indigenous Australians with AF were younger, and had low left ventricular systolic function and greater rates of cardiovascular comorbidities than non-Indigenous Australians with AF. They concluded that the risk factor modification may mitigate the excess burden of morbidity and mortality due to AF in younger Indigenous Australians. This is a large population study included over 200,000 patients during over 10 years in spite of some limitations.

Major comment
1. As the authors described, this study has limitations regarding to a selection bias, a discrepancies of number and characteristics of each group, diagnostic methods for AF and other structural heart disease, or omitting multiple strong comorbid factors associated with AF. Therefore, the authors need to mention that the results of this study could not be generalized.

We agree that the generalisability of our results are limited as a result of the above-mentioned factors, and have now included this more explicitly in the manuscript.

2. This is the cross sectional observation study, and there is no data explaining the relationship between AF prevalence and morbidity/ mortality. Also, the terminology of "Predictor" in multivariable

analysis should be changed to the “association”. The need for better primary prevention strategies is also speculative. The authors should tone down the conclusion based on the data.

We have changed the terminology to associations as suggested, and have reworded the conclusion to be more circumspect regarding the need for preventative strategies.

Minor Comments
1. Although the authors described the difference between Indigenous Australians and non-Indigenous Australians regarding to the medical aspects, the readers may have curiosity whether it is related to genetic factor or their life-style. I recommend discuss more about the characteristics for Indigenous Australians.

We agree that there are multiple possible factors that may in-part be contributing to the observed findings in our study, including genetic and lifestyle factors. We have bolstered the discussion on potential genetic aspects and noted the absence of any studies on genetic factors including Indigenous Australians to the best of our knowledge. We have similarly better discussed the differences in broad risk factor profiles which reflect entrenched social, economic and educational disadvantage which, in-turn, influence many life-style factors.

2. The logic of the authors seems to be Indigenous Australians are different to non-Indigenous Australians genetically, so that the prevalence of structural heart disease or remodeling are different, resulting in high prevalence of young age AF. Therefore, early intervention for primary prevention in this group will reduce the risk of AF and other cardiovascular conditions. However, there are too many steps of speculation to support this complicated logics. Propensity score matching of control group to Indigenous Australians may be helpful to support the authors’ explanation with this precious large population data.

We thank the reviewer for his suggestion. As above, we agree that multiple possible factors, including genetic differences and varying risk factor profiles, may be in part responsible for the high prevalence of AF in young Indigenous Australians. We believe that the association observed between Indigenous Australian status and prevalent AF in univariate, but not multivariate-adjusted, regression models supports our belief that varying risk factor profiles may, at least in-part, explain our findings. We thus would like to respectfully retain our current analyses and have attempted to better explain this logic.

3. Did structural changes of hear induce AF, or AF induced structural remodeling of heart? Although it is not possible to document the causal-result relationship, please discuss about that.

We agree that it would not be difficult to conclude whether patients structural changes and due to or causing AF. As a result, we excluded patients with AF from our echocardiographic analysis and have made this more explicit in the manuscript to reflect this fact.

Reviewer Name MANSOURATI, Jacques
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Please state any competing interests or state ‘None declared’: None declared

This is a retrospective study with its limitations some additional clinical data may have been

interesting

This paper brings interesting and original epidemiological results on AF in 2 australian populations.
It may have preventive impact on Indigenious population according to the results.
The study is however retrospective and has to be analyzed carefully It would have been interesting to have more clinical data on the studied populations as body mass index and alcohol consumption.
Would that be still possible? These parameters may bring a possible explanation for the results

We thank the reviewer for the helpful suggestions, and agree that other clinical data such as body mass index and alcohol consumption are relevant factors. We unfortunately do not have access to such data but have included these in the discussion and limitation sections.